

SEQUENCE LISTING

<110> DAVIS, SIMON

<120> RECEPTOR MODULATORS

<130> ISI.103

<140> US 10/585,491

<141> 2006-07-07

<150> PCT/GB05/000099

<151> 2005-01-10

<150> GB 0400440.4

<151> 2004-01-09

<150> US 60/536,354

<151> 2004-01-14

<160> 61

<170> PatentIn version 3.2

<210> 1

<211> 220

<212> PRT

<213> Homo sapiens

<220>

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<222> (1)..(220)

<223> HUMAN CD28

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Met Leu Arg Leu Leu Ala Leu Asn Leu Phe Pro Ser Ile Gln Val
1 5 10 15

Thr Gly Asn Lys Ile Leu Val Lys Gln Ser Pro Met Leu Val Ala Tyr
20 25 30

Asp Asn Ala Val Asn Leu Ser Cys Lys Tyr Ser Tyr Asn Leu Phe Ser
35 40 45

Arg Glu Phe Arg Ala Ser Leu His Lys Gly Leu Asp Ser Ala Val Glu
50 55 60

Val Cys Val Val Tyr Gly Asn Tyr Ser Gln Gln Leu Gln Val Tyr Ser
65 70 75 80

Lys Thr Gly Phe Asn Cys Asp Gly Lys Leu Gly Asn Glu Ser Val Thr
85 90 95

Phe Tyr Leu Gln Asn Leu Tyr Val Asn Gln Thr Asp Ile Tyr Phe Cys
100 105 110

Lys Ile Glu Val Met Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys Ser
 115 120 125

Asn Gly Thr Ile Ile His Val Lys Gly Lys His Leu Cys Pro Ser Pro
 130 135 140

Leu Phe Pro Gly Pro Ser Lys Pro Phe Trp Val Leu Val Val Val Gly
 145 150 155 160

Gly Val Leu Ala Cys Tyr Ser Leu Leu Val Thr Val Ala Phe Ile Ile
 165 170 175

Phe Trp Val Arg Ser Lys Arg Ser Arg Leu Leu His Ser Asp Tyr Met
 180 185 190

Asn Met Thr Pro Arg Arg Pro Gly Pro Thr Arg Lys His Tyr Gln Pro
 195 200 205

Tyr Ala Pro Pro Arg Asp Phe Ala Ala Tyr Arg Ser
 210 215 220

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<223> CD28/Fc fusion protein

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Met Asp Trp Leu Arg Asn Leu Leu Phe Leu Met Ala Ala Ala Gln Ser
 1 5 10 15

Ile Asn Ala Asn Lys Ile Leu Val Lys Gln Ser Pro Met Leu Val Ala
 20 25 30

Tyr Asp Asn Ala Val Asn Leu Ser Cys Lys Tyr Ser Tyr Asn Leu Phe
 35 40 45

Ser Arg Glu Phe Arg Ala Ser Leu His Lys Gly Leu Asp Ser Ala Val
 50 55 60

Glu Val Cys Val Val Tyr Gly Asn Tyr Ser Gln Gln Leu Gln Val Tyr
 65 70 75 80

Ser Lys Thr Gly Phe Asn Cys Asp Gly Lys Leu Gly Asn Glu Ser Val
 85 90 95

Thr Phe Tyr Leu Gln Asn Leu Tyr Val Asn Gln Thr Asp Ile Tyr Phe
 100 105 110

Cys Lys Ile Glu Val Met Tyr Pro Pro Pro Tyr Leu Asp Asn Glu Lys

115	120	125
Ser Asn Gly Thr Ile Ile His Val Lys Gly Lys His Leu Cys Pro Ser		
130	135	140
Pro Leu Phe Pro Gly Pro Ser Lys Pro Leu Val Pro Arg Gly Ser Gly		
145	150	155
160		
Ser Lys Pro Ser Ile Ser Thr Val Pro Glu Val Ser Ser Val Phe Ile		
165	170	175
Phe Pro Pro Lys Pro Lys Asp Val Leu Thr Ile Thr Leu Thr Pro Lys		
180	185	190
Val Thr Cys Val Val Asp Ile Ser Lys Asp Asp Pro Glu Val Gln		
195	200	205
Phe Ser Trp Phe Val Asp Asp Val Glu Val His Thr Ala Gln Thr Gln		
210	215	220
Pro Arg Glu Glu Gln Phe Asn Ser Thr Phe Arg Ser Val Ser Glu Leu		
225	230	235
240		
Pro Ile Met His Gln Asp Trp Leu Asn Gly Lys Glu Phe Lys Cys Arg		
245	250	255
Val Asn Ser Ala Ala Phe Pro Ala Pro Ile Glu Lys Thr Ile Ser Lys		
260	265	270
Thr Lys Gly Arg Pro Lys Ala Pro Gln Val Tyr Thr Ile Pro Pro Pro		
275	280	285
Lys Glu Gln Met Ala Lys Asp Lys Val Ser Leu Thr Cys Met Ile Thr		
290	295	300
Asp Phe Phe Pro Glu Asp Ile Thr Val Glu Trp Gln Trp Asn Gly Gln		
305	310	315
320		
Pro Ala Glu Asn Tyr Lys Asn Thr Gln Pro Ile Met Asp Thr Asp Gly		
325	330	335
Ser Tyr Phe Val Tyr Ser Lys Leu Asn Val Gln Lys Ser Asn Trp Glu		
340	345	350
Ala Gly Asn Thr Phe Thr Cys Ser Val Leu His Glu Gly Leu His Asn		
355	360	365
His His Thr Glu Lys Ser Leu Ser His Ser Pro Gly Lys		
370	375	380

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<210> 6
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<400> 6
Tyr Xaa Tyr Xaa Xaa Xaa
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<210> 7
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Tyr Xaa Tyr Xaa Xaa Xaa
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<210> 8
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<400> 8

Tyr Xaa Tyr Xaa Xaa
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Xaa
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<222> (6)..(6)
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<400> 9
Xaa Xaa Tyr Xaa Xaa Xaa
1 5

<210> 10
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Thr Xaa Tyr Xaa Xaa Xaa
1 5

<210> 11
<211> 57
<212> DNA
<213> Artificial sequence

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<223> OLIGONUCLEOTIDE PRIMER

<400> 11
tagtagtcta gaccccatcc gctcaagcag gccaccatgg attggctcg gaacttg

57

<210> 12
<211> 31
<212> DNA
<213> Artificial sequence

<220>
<223> OLIGONUCLEOTIDE PRIMER

<400> 12
ctaccactac ccctgggtac caggggctta g

31

<210> 13
<211> 31
<212> DNA
<213> Artificial sequence

<220>
<223> OLIGONUCLEOTIDE PRIMER

<400> 13
ctaagcccc ggtacccagg ggtagtggtta g

31

<210> 14
<211> 34
<212> DNA
<213> Artificial sequence

<220>

<223> OLIGONUCLEOTIDE PRIMER

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ctactatcta gattatttac caggagagtg ggag		34
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<211> 1514		
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<213> Homo sapiens		
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gaggaggggc tggaacccta gcccatcgta aggacaaaga tgctcaggct gctttggct	120	
ctcaacttat tcccttcaat tcaagtaaca ggaaacaaga ttttggtgaa gcagtcgccc	180	
atgctttagt cgtacgacaa tgcggtcaac cttagctgca agtattccta caatctttc	240	
tcaaggagt tccgggcatc cttcacaaa ggactggata gtgctgtgaa agtctgtgtt	300	
gtatatggaa attactccca gcagcttcag gtttactcaa aaacggggtt caactgtgat	360	
ggaaattgg gcaatgaatc agtgacattc tacctccaga atttgtatgt taaccaaaca	420	
gatatttact tctgcaaaat tgaagttatg tatccttcctc cttacctaga caatgagaag	480	
agcaatggaa ccattatcca tgtgaaagg aaacaccttt gtccaagtcc octatccc	540	
ggaccttcta agccctttt ggtgctggtg gtgggtggtg gagtcctggc ttgctatagc	600	
ttgctagtaa cagtggcattt tatttttc tgggtgagga gtaagaggag caggtcctg	660	
cacagtgact acatgaacat gactccccgc cgccccggc ccacccgcaa gcattaccag	720	
ccctatgccc caccacgca ctgcgcagcc tatcgctct gacacggacg octatccaga	780	
agccagccgg ctggcagccc ccatctgctc aatatcaactg ctctggatag gaaatgaccg	840	
ccatctccag ccggccacct cagccccgt tggccacca atgccaattt ttctcgatgt	900	
actagaccaa atatcaagat catttgaga ctctgaaatg aagtaaaaga gatttcctgt	960	
gacaggccaa gtcttacagt gccatggccc acattccaaac ttaccatgtt cttagtgact	1020	
tgactgagaa gttaggtag aaaacaaaaa gggagtggat tctggagcc tcttcccttt	1080	
ctcaactcacc tgcacatctc agtcaagcaa agtgtggat ccacagacat ttttagttgca	1140	

gaagaaaggc taggaaatca ttccctttgg ttaaatgggt gttaatctt ttggtagtg	1200
ggtaaacgg ggtaagttag agtaggggaa gggataggaa gacatattta aaaaccatta	1260
aaacactgtc tcccactcat gaaatgagcc acgtagttcc tatttaatgc tgccccctt	1320
tagtttagaa atacatagac attgtctttt atgaattctg atcatattta gtcattttga	1380
ccaaatgagg gatttggtca aatgagggat tccctcaaag caatatcagg taaaccaagt	1440
tgcccccctc actccctgtc atgagacttc agtgttaatg ttcacaatat actttcgaaa	1500
gaataaaata gttc	1514

<210> 16
<211> 1170
<212> DNA
<213> Artificial sequence

<220>
<223> CD28TFc SEQUENCE

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gccgctcaaa gtatcaacgc gaacaagatc ttggtaagc agtcgccccat gctttagcg	120
tacgacaatg cggtaacct tagctgcaag tattcctaca atctttctc aaggagttc	180
cgggcatccc ttcacaaagg actggatagt gctgtggaag tctgtgttgt atatggaat	240
tactcccagc agcttcaggt ttactcaaaa acggggttca actgtgatgg gaaattgggc	300
aatgaatcag tgacattcta cctccagaat ttgtatgtta accaaacaga tatttacttc	360
tgcaaaattt aagttatgtt tacctccttct tacctagaca atgagaagag caatggtacc	420
attatccatg tgaaaggaa acacctttgt ccaagtccgc tatttcccg accttctaag	480
cccttggtag ccagggtag tggtagtaag cctagcataa gtacagtccc agaagtatca	540
tctgtcttca tcttcccccc aaagcccaag gatgtgctca ccattactct gactcctaag	600
gtcacgtgtg ttgtggtaga catcagcaag gatgatcccc aggtccagtt cagctggtt	660
gttagatgtg tggaggtgca cacagctcag acgcaacccc gggaggagca gttcaacagc	720
actttccgct cagtcagtga acttcccatc atgcaccagg actggctcaa tggcaaggag	780
ttcaaatgca gggtaacag tgcagcttcc cctgccccca tcgagaaaac catctccaaa	840
accaaaggca gaccgaaggc tccacaggtg tacaccatc cacctcccaa ggagcagatg	900
gccaaggata aagtcagtct gacctgcattg ataacagact tcttccctga agacattact	960

gtggagtggc agtggaatgg gcagccagcg gagaactaca agaacactca gcccatcatg	1020
gacacagatg gctcttactt cgtctacagc aagctcaatg tgcagaagag caactggag	1080
gcagggaaata ctttcacctg ctctgtgtta catgagggcc tgcacaacca ccatactgag	1140
aagagctct cccactctcc tggtaaataa	1170

<210> 17
<211> 115
<212> PRT
<213> Homo sapiens

<220>
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<222> (1)..(115)
<223> HUMAN CTLA-4

<400> 17			
Ala Met His Val Ala Gln Pro Ala Val Val Leu Ala Ser Ser Arg Gly			
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Ile Ala Ser Phe Val Cys Glu Tyr Ala Ser Pro Gly Lys Ala Thr Glu		
20	25	30

Val Arg Val Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val		
35	40	45

Cys Ala Ala Thr Tyr Met Met Gly Asn Glu Leu Thr Phe Leu Asp Asp		
50	55	60

Ser Ile Cys Thr Gly Thr Ser Ser Gly Asn Gln Val Asn Leu Thr Ile			
65	70	75	80

Gln Gly Leu Arg Ala Met Asp Thr Gly Leu Tyr Ile Cys Lys Val Glu		
85	90	95

Leu Met Tyr Pro Pro Tyr Tyr Leu Gly Ile Gly Asn Gly Thr Gln		
100	105	110

Ile Tyr Val
115

<210> 18
<211> 110
<212> PRT
<213> Homo sapiens

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<222> (1)..(110)

<223> HUMAN ICOS

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Gly	Val	Gln	Ile	Leu	Cys	Lys	Tyr	Pro	Asp	Ile	Val	Gln	Gln	Phe	Lys
									25					30	
Met	Gln	Leu	Leu	Lys	Gly	Gln	Ile	Leu	Cys	Asp	Leu	Thr	Lys	Thr	
									40				45		
Lys	Gly	Ser	Gly	Asn	Thr	Val	Ser	Ile	Lys	Ser	Leu	Lys	Phe	Cys	His
									55			60			
Ser	Gln	Leu	Ser	Asn	Asn	Ser	Val	Ser	Phe	Phe	Leu	Tyr	Asn	Leu	Asp
									70		75		80		
His	Ser	His	Ala	Asn	Tyr	Tyr	Phe	Cys	Asn	Leu	Ser	Ile	Phe	Asp	Pro
									85		90		95		
Pro	Pro	Phe	Lys	Val	Thr	Leu	Thr	Gly	Gly	Tyr	Leu	His	Ile		
								100		105		110			

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<223>	HUMAN PD-1			

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Ala	Thr	Phe	Thr	Cys	Ser	Phe	Ser	Asn	Thr	Ser	Glu	Ser	Phe	Val	Leu	
									20		25		30			
Asn	Trp	Tyr	Arg	Met	Ser	Pro	Ser	Asn	Gln	Thr	Asp	Lys	Leu	Ala	Ala	
									35		40		45			
Phe	Pro	Glu	Asp	Arg	Ser	Gln	Pro	Gly	Gln	Asp	Cys	Arg	Phe	Arg	Val	
									50		55		60			
Thr	Gln	Leu	Pro	Asn	Gly	Arg	Asp	Phe	His	Met	Ser	Val	Val	Arg	Ala	
									65		70		75		80	
Arg	Arg	Asn	Asp	Ser	Gly	Thr	Tyr	Leu	Cys	Gly	Ala	Ile	Ser	Leu	Ala	
									85		90		95			
Pro	Lys	Ala	Gln	Ile	Lys	Glu	Ser	Leu	Arg	Ala	Glu	Leu	Arg			

100 105 110

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<211> 106
<212> PRT
<213> Homo sapiens

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<223> HUMAN IgL-KAPPA

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Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg
1 5 10 15

Val Thr Phe Thr Cys Arg Ser Ser Gln Thr Ile Gly Thr Tyr Leu Asn
20 25 30

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Lys Leu Leu Ile Phe Ala
35 40 45

Ala Ser Ser Leu Leu Asn Gly Val Pro Ser Arg Phe Ser Gly Ser Gly
50 55 60

Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp
65 70 75 80

Phe Ala Thr Tyr Tyr Cys Gln Gln Ser His Ser Ala Pro Pro Tyr Thr
85 90 95

Phe Gly Gln Gly Thr Arg Leu Glu Met Lys
100 105

<210> 21
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<213> Homo sapiens

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<222> (1)..(108)
<223> HUMAN TCR ALPHA

<400> 21
Gln Val Glu Gln Ser Pro Pro Asp Leu Ile Leu Gln Glu Gly Ala Asn
1 5 10 15

Ser Thr Leu Arg Cys Asn Phe Ser Asp Ser Val Asn Asn Leu Gln Trp
20 25 30

Phe His Gln Asn Pro Trp Gly Gln Leu Ile Asn Leu Phe Tyr Ile Pro
35 40 45

Ser Gly Thr Lys Gln Asn Gly Arg Leu Ser Ala Thr Thr Val Ala Thr
 50 55 60

Glu Arg Tyr Ser Leu Leu Tyr Ile Ser Ser Ser Gln Thr Thr Asp Ser
 65 70 75 80

Gly Val Tyr Phe Cys Ala Ala Leu Asp Leu Trp Gly Gly Ala Asp Gly
 85 90 95

Leu Thr Phe Gly Lys Gly Thr His Leu Ile Ile Gln
 100 105

<210> 22

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<212> PRT

<213> Homo sapiens

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<221> MISC_FEATURE

<222> (1)..(98)

<223> HUMAN BTLA

<400> 22

Gln Leu Tyr Ile Lys Arg Gln Ser Glu His Ser Ile Leu Ala Gly Asp
 1 5 10 15

Pro Phe Glu Leu Glu Cys Pro Val Lys Tyr Cys Ala Asn Arg Pro His
 20 25 30

Val Thr Trp Cys Lys Leu Asn Gly Thr Thr Cys Val Lys Leu Glu Asp
 35 40 45

Arg Gln Thr Ser Trp Lys Glu Glu Lys Asn Ile Ser Phe Phe Ile Leu
 50 55 60

His Phe Glu Pro Met Leu Pro Asn Asp Asn Gly Ser Tyr Arg Cys Ser
 65 70 75 80

Ala Asn Phe Gln Ser Asn Leu Glu Ser His Ser Thr Thr Leu Tyr
 85 90 95

Val Thr

<210> 23

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> hCD28 epitope

<400> 23

Ser Pro Met Leu Val
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<210> 24
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> hCTLA-4 epitope

<400> 24

Pro Ala Val Val Leu
1 5

<210> 25
<211> 5
<212> PRT
<213> Artificial sequence

<220>
<223> hICOS epitope

<400> 25

Tyr Glu Met Phe Ile
1 5

<210> 26
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> hCD28 epitope

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Ala Val Asn Leu Ser
1 5

<210> 27
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<212> PRT
<213> Artificial sequence

<220>
<223> hCTLA-4 epitope

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Gly Ile Ala Ser Phe Val
1 5

<210> 28
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<212> PRT
<213> Artificial sequence

<220>
<223> hICOS epitope

<400> 28

Gly Val Gln Ile Leu
1 5

<210> 29
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<212> PRT
<213> Artificial sequence

<220>
<223> hCD28 epitope

<400> 29

Ser Leu His Lys Gly Leu Asp Ser Ala Val Glu Val Cys Val
1 5 10

<210> 30
<211> 15
<212> PRT
<213> Artificial sequence

<220>
<223> hCTLA-4 epitope

<400> 30

Thr Val Leu Arg Gln Ala Asp Ser Gln Val Thr Glu Val Cys Ala
1 5 10 15

<210> 31
<211> 11
<212> PRT
<213> Artificial sequence

<220>
<223> hICOS epitope

<400> 31

Gln Leu Leu Lys Gly Gly Gln Ile Leu Cys Asp
1 5 10

<210> 32

<211> 11

<212> PRT

<213> Artificial sequence

<220>

<223> hCD28 epitope

<400> 32

Val Tyr Ser Lys Thr Gly Phe Asn Cys Asp Gly
1 5 10

<210> 33

<211> 9

<212> PRT

<213> Artificial sequence

<220>

<223> hCTLA-4 epitope

<400> 33

Phe Leu Asp Asp Ser Ile Cys Thr Gly
1 5

<210> 34

<211> 11

<212> PRT

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<220>

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<400> 34

Val Ser Ile Lys Ser Leu Lys Phe Cys His Ser
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Phe Tyr Leu Gln Asn

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Leu Thr Ile Gln Gly

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Phe Phe Leu Tyr Asn

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Thr Asp Ile Tyr Phe Cys

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Thr Gly Gly Tyr Leu His Ile
1 5

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Pro Ala Leu Leu Val Val
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Gln Ser Glu His Ser Ile
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Asp Asn Ala Thr Phe
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Asp Pro Phe Glu Leu
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<210> 48

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Arg Met Ser Pro Ser Asn Gln Thr Asp Lys
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Lys Leu Asn Gly
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Gln Pro Gly Gln Asp Cys Arg Phe Arg
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Gln Thr Ser Trp Lys
1 5

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Met Ser Val Val Arg
1 5

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Leu His Phe Glu Pro
1 5

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Asn Asp Ser Gly Thr Tyr
1 5

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Asn Asp Asn Gly Ser Tyr
1 5

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Leu Arg Ala Glu Leu Arg
1 5

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Thr Thr Leu Tyr Val Thr
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<210> 59
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<400> 59

Tyr Met Met Gly Asn Glu Leu Thr Phe Leu Asp Asp Ser
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Lys Thr Lys Gly Ser Gly Asn Thr Val Ser Ile Lys Ser Leu Lys
1 5 10 15

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Leu Ala Ala Phe Pro Glu Asp Arg Ser Gln Pro Gly Gln Asp Cys Arg
1 5 10 15